

REMARKS

Withdrawn Claims

Claims 22 and 23 are noted withdrawn in the Office Action. These claims are dependent claims from the non-withdrawn claims, and thus, should not have been withdrawn. Their consideration is requested.

Abstract

Applicant's copy of the filed application contains an abstract. Thus, the PTO version of the application should also contain the same abstract. Nevertheless, an abstract is attached.

The Rejections Under 35 USC § 112, second paragraph

The Office Action alleges that in claim 4, the term "alkoxy-phenyl-benzodiazepine" is undefined because it is not stated where the substituents are placed. The term "alkoxy-phenyl-benzodiazepine" is meant to define all possible substitutions on an alkoxy-phenyl-benzodiazepine compound as all have antagonistic properties at AMPA receptors. There is no indefiniteness. Compounds, which are all included in the definition of alkoxy-phenyl-benzodiazepine, are, for example, 7,8-(methylenedioxy)-1-phenyl-3,5-dihydro-4H-2,3-benzodiazepin-4-ones (J. Med. Chem. 1998; 41, 2621-2625); condensed 2,3-benzodiazepine derivatives as listed in WO 97/28163; 5H-2,3-benzodiazepines as listed on WO 0198280 A2; 3-acetyl-1-(4-amino-3-methyl-phenyl)-4,5-dihydro-8-chloro-4-methyl-3H-2,3-benzodiazepines as listed in WO 200250044-A1; 8-substituted-9H-1,3-dioxolo[4,5-h]/2,3/benzodiazepine derivatives as listed in WO 99/07707; 1,3-Dioxolo[4,5-h]/2,3/benzodiazepine derivatives as listed in WO 99/07708; and 2,3-benzodiazepine derivatives listed in the publication by Tarnawa and Vizi, Restorative Neurology and Neuroscience 13(1998), 41-57.

The Rejections Under 35 USC § 103

Claims 1-7 were alleged to be unpatentable over Gonoï et al in view of Yoshioka et al and in further view of Fletcher et al.

Gonoï et al as admitted by the Office Action, do not teach the use of AMPA antagonists to treat tumor progression. In fact, if anything, Gonoï et al teaches the opposite.

Gonoï et al investigates the expression of glutamate receptor agonists in insulinoma cell

line MIN6. Gonoï et al teach that agonists at glutamate receptors increase intracellular calcium concentration in MIN6 cells. See page 16990, last two lines to page 16991, first three lines. Gonoï et al also comment that in cells expressing glutamate receptors, extracellular glutamate is expected to cause cell death, but that the MIN6 cells avoided cell death. See page 16991, last eight lines.

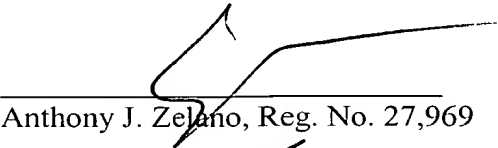
Thus, if anything, Gonoï et al teach to one of ordinary skill in the art that agonists at glutamate receptors normally lead to cell death. Based on this, one of ordinary skill in the art would conclude that if agonists normally lead to cell death, antagonists would have the opposite effect, and, thus, not be useful, e.g., to treat cancer. For this reason alone, this can be no obviousness irrespective of the secondary references.

Yoshioka et al, at best, is neutral on this teaching away of Gonoï et al. If a cell were not susceptible to the excitotoxicity form of cell death, as the Examiner notes, i.e., to this glutamate receptor pathway of causing cell death, then glutamate receptor active compounds (agonist and antagonists) would be ineffective for causing or blocking excitotoxicity mediated cell death. Thus, Yoshioka et al. cannot be combined with Gonoï et al. to suggest the claimed invention. (Yoshioka et al examined the effect of a variety of NMDA and non-NMDA agonists on a variety of cell lines and teaches that some of the cell lines fail to assemble Ca^{2+} permeable NMDA or non-NMDA glutamate receptor channels, which failure is taught to protect against excitotoxicity and which may contribute to progression of tumors of certain types. See page 171, last paragraph and abstract. This is consistent with Gonoï et al. The Office Action also alleges that Yoshioka et al teaches that “Cellular excitotoxicity has been demonstrated to occur through glutamate-gated ionotropic receptors and blocked by antagonists to glutamate-gated ionotropic receptors (pg. 164, 2nd paragraph in Introduction section).” Applicants do not see where Yoshioka et al teaches the alleged material. Nevertheless, such a statement again would only confirm the teaching away by Gonoï et al, i.e., that antagonists block excitotoxicity and, hence, do not effect desired cell death.)

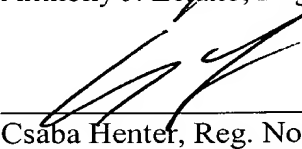
Fletcher and Oftebro et al. are irrelevant to the defects noted above in the rejection and thus do not render the claims obvious in combination with the other references.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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